

[Chem. Pharm. Bull., 45, 384-388 (1997)]

[Lab. of Pharm. Engineering]

**Penetration of Outer Layered Particles of Agglomerate into Inner Interstices
of Agglomerate during Spherical Agglomeration in Liquid.**

Yoshiaki KAWASHIMA,* Kouji NIWA, Hirofumi TAKEUCHI and Tomoaki HINO

Layering agglomeration of aluminum lake particles was conducted by depositing them on a cored agglomerate of lactose prepared by the wet spherical agglomeration technique with a bridging liquid in a dispersing medium under agitation. The layered agglomerates were spheronized and compacted during agglomeration. The processes of layering agglomeration and compaction are as described by the selective coalescence mechanism proposed by Kapur and a modified Kawakita's equation. It was newly found that the aluminum lake particles layered on the surface of core agglomerate penetrated gradually into the inside of core agglomerates during agglomeration. The penetration behaviors of aluminum lake particles were represented by their relative movement coefficients, found by measuring their distributions in the agglomerate with a color measuring system. The mechanism of penetration of aluminum lake particles was discussed by referring to the tapping processes of aluminum lake and lactose powders in liquid and air.

[Int. J. Pharm., 149, 43-49 (1997)]

[Lab. of Pharm. Engineering]

**Influence of the Degrees of Hydrolyzation and Polymerization of
Poly(vinylalcohol) on the Preparation and Properties of Poly(DL-lactide-co-
glycolide) nanoparticle.**

Hideki MURAKAMI, Yoshiaki KAWASHIMA,* Toshiyuki NIWA, Tomoaki HINO,
Hirofumi TAKEUCHI and Masao KOBAYASHI

The influences of the degrees of hydrolyzation and polymerization of poly(vinylalcohol) (PVA) used as an emulsion stabilizer were investigated on the preparation of poly(DL-lactide-co-glycolide) (PLGA) nanoparticles. It was found that the degree of hydrolyzation of PVA was more important than the degree of polymerization to improve productivity and physical properties. A series of gelatinization studies of PVA suggested that the localized gelatinization of PVA preferentially occurred on the surface of emulsion droplets containing PLGA in the solvent diffusion process, thus influencing the formability of PLGA nanoparticles.

[Drug Delivery System, 12, 161-165 (1997)]

[Lab. of Pharm. Engineering]

**Evaluation of Acute Toxicity of Epirubicin Hydrochloride-encapsulating
w/o/w Emulsion Administered to Rat for the Transcatheter Embolization
Therapy for Hepatocellular Carcinoma.**

Tomoaki HINO, Makiko ISOZAKI, Hiromitsu YAMAMOTO, Hirofumi TAKEUCHI, Yoshiaki KAWASHIMA,*
Satoshi NAKANO, Futoshi YAMAZAKI, Takashi KUMADA and Toshi SASSA

The toxicity of lipiodol(LPD) w/o/w emulsions encapsulating epirubicin hydrochloride (FARM) after iv administration to rat was investigated compared to the conventional o/w emulsions used for transcatheter arterial embolization(TAE) therapy for hepatocellular carcinoma. Survival time of the rat administered w/o/w emulsion was longer than that of the o/w emulsion. The rats administered o/w emulsion were deceased within 2 days by pulmonary edema caused by embolism with fine oil droplets. The edema was not found in the lungs of the rats administered w/o/w emulsion.

[Drug Delivery System, 12, 347-352 (1997)]

[Lab. of Pharm. Engineering]

**Protective Effects of Chitosan and Liposomal Formulation for Enzymatic
Degradation of Insulin and Their Absorption Promoting Effects in Intestinal
Mucous Layer.**

Hirofumi TAKEUCHI, Yuka SHIMOTORI, Hiromitsu YAMAMOTO,
Tomoaki HINO and Yoshiaki KAWASHIMA*

In this study, we investigated protective effects of chitosan and liposomal formulation on enzymatic degradation of insulin and promoting effect of chitosan in absorption of insulin in the gastrointestinal tract. In assessing absorption promoting effects of chitosan, pulse chaser test was carried out. As the total protein concentration in mucous layer homogenate was increased, the degradation rate of insulin in the solution was accelerated. The enzymatic degradation of insulin was protected in the presence of chitosan or liposomal encapsulation supposed to be important in protecting enzymatic degradation of insulin, because carboxymethyl chitin, which possesses a similar structure with chitosan but has no free amino groups, showed little protective effects.